



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2017-D-1846]

**Labeling for Combined Hormonal Contraceptives; Draft Guidance for Industry;
Availability**

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Labeling for Combined Hormonal Contraceptives.” This draft guidance provides recommendations on information that should be included in the prescribing information for combined hormonal contraceptives (CHCs), which contain estrogen and progestin. CHC products include combined oral contraceptives (COCs), as well as non-oral products such as transdermal systems and vaginal rings. Many of the labeling recommendations in this draft guidance represent class labeling that should be included in all CHC prescribing information. The draft guidance reflects many of the modifications to prescribing information mandated by the physician labeling rule (PLR) and the pregnancy and lactation labeling rule (PLLR). General advice is provided where modifications to the prescribing information for specific products are needed.

DATES: Submit either electronic or written comments on the draft guidance by **[INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]** to

ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2017-D-1846 for “Labeling for Combined Hormonal Contraceptives; Draft Guidance for Industry.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015,

or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Jennifer Dao, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 5333, Silver Spring, MD 20993-0002, 301-796-8189.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Labeling for Combined Hormonal Contraceptives.” This draft guidance provides recommendations on information that should be included in the prescribing information for CHCs, which contain estrogen and a progestin. Such products include COCs, as well as non-oral products such as

transdermal systems and vaginal rings. Many of the labeling recommendations in this draft guidance represent class labeling that should be included in all CHC prescribing information. The draft guidance reflects many of the modifications to prescribing information mandated by the PLR¹ and the PLLR.² General advice is provided where modifications of the prescribing information for specific products are needed.

FDA previously issued draft guidance on the prescribing information for COCs in March 2004 and invited public comment. That draft guidance was withdrawn in July 2015. However, the development of the current draft guidance took into consideration public comments submitted to the 2004 draft guidance that were science-based and consistent with current PLR and PLLR labeling regulations. This draft guidance has been broadened to incorporate the more general class of CHCs.

FDA invites comments on the content of this draft guidance. In particular, FDA seeks comments on the proposed language under section 7.1 of labeling that identifies a drug interaction with all metabolic enzyme inducers. A variety of metabolic enzyme inducers have been reported to decrease the plasma concentration of the estrogen and/or progestin components of CHCs. FDA seeks comments and data regarding specific enzyme inducers or classes of inducers (e.g., cytochrome p450 3A strong inducers) that interact with CHCs; in particular,

¹ See the final rule “Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products” (71 FR 3922, January 24, 2006) (21 CFR 201.56(d)(1) and 201.57(c)(9)(i) through (iii)); see also the guidance for industry entitled “Labeling for Human Prescription Drug and Biological Products--Implementing the PLR Content and Format Requirements” available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075082.pdf>.

² See the final rule “Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling” (79 FR 72064, December 4, 2014) (21 CFR 201.56(d) and 201.57); see also the draft guidance for industry entitled “Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products--Content and Format” available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM425398.pdf>. When final, this guidance will represent FDA’s current thinking on this topic.

comments are requested on whether the CHC labeling should include specific inducers or classes of inducers, or if it should remain broad and essentially cover all possible cytochrome p (CYP) enzyme inducers of any pathway and potency.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on labeling for CHCs. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. This guidance is not subject to Executive Order 12866.

II. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR 201.56 and 201.57 ("Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products") are approved under OMB control number 0910-0572. The collections of information from the final rule entitled "Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling" are approved under OMB control number 0910-0624.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at either <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <https://www.regulations.gov/>.

Dated: December 26, 2017.

Leslie Kux,

Associate Commissioner for Policy.

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